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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,502	02/05/2004	David B. Rozema	Mirus.042.03	5669

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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/18/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,502	ROZEMA ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/04/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of group II in the reply filed on 10/20/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-12 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/20/06.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 13, 16-17, and 22-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-13, 18-21 of U.S. Patent No. 7,098,032. Although the conflicting claims are not identical, they are

not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). The MPEP states, at §804, that:

> [t]he specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

The instant claim in each instance is more narrowly drawn than the corresponding patented claim. However, the portion of US Patent 7,098,032 that supports each of claims 13, 16-17, and 22-25 defines the patented invention as including embodiments which possess each of the narrower limitations of the instant claims. Thus, the inventions of the instant claims are not patentably distinct from those of respective patented claims 11-13, 18-21. Polyvinylethers recited in the instant claims are defined

as part of the invention of the patented claims in which the polyanions of the claims are prepared using 2-chloroethyl vinyl ether in Example 2.

Claim Objections

5. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

There are two claims numbered as #28. Misnumbered claims 28, 28 and 29 been renumbered claims 28, 29, and 30 respectively.

6. Claim 18 is objected to because of the following informalities: Claim 18 is not grammatically correct. Claim 18 should use the article "an" before "amphiphilic polyvinylether". Appropriate correction is required.

7. Claim 20 is objected to because of the following informalities: Claim 20 is not grammatically correct. Claim 20 should use the article "an" before "anionic polyvinylether". Appropriate correction is required.

8. Claim 21 is objected to because of the following informalities: Claim 21 is not grammatically correct. Claim 21 should use the article "an" before "amphiphilic polyvinylether". Appropriate correction is required.

Specification

9. The disclosure is objected to because of the following informalities:

10. The first sentence of the specification is missing a period at the end of the sentence, page 1, line 7.

11. There is a misplaced comma, instead of a period at the end of a sentence on page 3, line 24.

12. The word "deliver" is misspelled "delivery" on page 3, line 29.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 13-22, and 25-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Meier et al (US Patent No: 6,616,946). Claims 13-22, and 25-30 recite a composition for the delivery of a polynucleotide to a cell comprising the polynucleotide and a polyvinylether (claim 13). The composition is further limited wherein the polynucleotide is bound with the polyvinylether via and electrostatic interaction (claim 14) or a covalent linkage (claim 15) or a labile covalent linkage (claim 16). The

composition is further limited wherein the polyvinyl ether consists of a cationic (claim 17) or amphiphilic polyvinylether (claim 18). The composition further comprises a maleic anhydride modified polyvinylether (claim 19) and wherein the modified polyvinylether consists of an anionic polyvinylether (claim 20) or the modified polyvinylether consists of an amphiphilic polyvinylether (claim 21). The composition is further limited wherein the polynucleotide is selected from the list consisting of: DNA, plasmid DNA, linear DNA, double stranded DNA, single stranded DNA, RNA, an expression cassette, antisense oligonucleotide, siRNA, microRNA, RNA expression cassette, ribozyme, dsRNA, and synthetic polynucleotides (claim 22) or wherein the polynucleotide inhibits the expression of a gene in the cell (claim 25). The composition is further limited wherein the polyvinylether consists of a modified polyvinylether (claim 26) and wherein the modified polyvinyl ether consists of an anionic polyvinylether (claim 27) an amphiphilic polyvinylether (claim 28). The composition is further limited wherein the modification consists of a reversible modification (claim 29) and therein the polynucleotide is covalently linked to the polyvinyl ether (claim 30).

15. The specification fails to define "modified polyvinylether" in clear concise terms. In reading the specification, it appears that "modified polyvinylether" refers to a polyvinylether that has had functional groups added to the copolymer.

16. The specification fails to define "labile covalent linkage" in specific terms. In reading the specification, it appears that "labile covalent linkage" refers to covalent bonds that are reversible.

17. The specification fails to define "reversible modification". In reading the specification, it appears that "reversible modification" refers to the ability to remove the added functional groups.

18. The specification teaches, "[a]ntisense therapies hold tremendous promise for treating a wide variety of human diseases. These therapies are based on the selective inhibition of expression of a specific gene. Because they are highly specific, antisense agents could in theory have fewer side effects and display less toxicity than traditional drugs. In addition, because antisense agents exert their effects by binding to a complementary sequence in a target RNA molecule, designing antisense agents to specifically inhibit a particular RNA species is straightforward." (Page 16, lines 11-18).

19. Meier et al (US Patent No: 6,616,946) teaches a stimulus responsive hollow particle comprising copolymers (see abstract). Specifically Meier teaches that the copolymers comprise amphiphilic hydrophobic polyvinylether (column 9, lines 28-39) and amphiphilic hydrophilic polyvinylether (column 10, lines 6-13). Meier teaches these hollow polyvinylether copolymers further comprise biological agents, such as proteins, nucleic acids, and antisense oligonucleotides (column 15, lines 14-37). Since Meier teaches the transfer of antisense oligonucleotides into cells, and the specification details how antisense technology is used to inhibit gene expression in a cell, Meier teaches the polynucleotide inhibits expression of a gene in a cell. Meier teaches that the interaction between the agent and the polyvinylether is ionic (electrostatic) (column 18, lines 28-32) or through covalent bonds (column 18, lines 34-36).

20. Furthermore, Meier teaches that the polymers used in the hollow particles can be modified with a positive (cationic) or negative (ionic) charge (column 16, lines 43-45). Meier also teaches that the copolymers can be modified by the addition of maleic acid which renders the copolymers pH sensitive (column 6, lines 5-37). Meier teaches that the modified polyvinylether copolymers are rendered anionic with changes in pH (column 6, lines 5-37, particularly lines 29-31). Meier teaches that the formation of the hollow particles is a "result of the amphiphilic nature of the copolymers. The aggregation of the non-crosslinked particles occurs via non-covalent interactions and therefore is reversible" (column 8, lines 57-60). Additionally, Meier teaches that the hollow particles comprise degradable bonds (column 11, lines 37-46) and that "[degradable links or regions can be incorporated into the responsive polymer, or elsewhere into the structure of the hollow particles, so that the particles degrade over a period of time, such as after release of the active agent at the desired location" (column 16, lines 62-66). Since Meier teaches that the polynucleotides can be covalently linked to the core polyvinylether, he teaches that the bond can thus be a degradable (labile covalent) bond.

21. Thus Meier teaches an amphiphilic polyvinylether/polynucleotide composition wherein the polyvinylethers are ionic, cationic or anionic, and are reversibly modified by a maleic anhydride. Meier further teaches that the interaction between the polynucleotide is ionic, covalent or labile covalent. Thus Meier teaches the claimed invention.

Claim Rejections - 35 USC § 103

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. Claim 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meier et al (US Patent No: 6,616,946) in view of Merdan et al (Prospects for cationic polymers in gene and oligonucleotide therapy against cancer, Advanced Drug Delivery Reviews, 2002. 54:715-758). Claims 23-24 recite a composition for the delivery of a polynucleotide to a cell comprising the polynucleotide and a polyvinylether (claim 13) wherein the polynucleotide expresses a protein (claim 23) or wherein the polynucleotide expresses an RNA (claim 24).

24. Meier et al (US Patent No: 6,616,946) teaches a composition comprising a polynucleotide and a polyvinylether (see above). Meier does not teach that the polynucleotide expresses a protein, nor that the polynucleotide expresses an RNA.

25. Merdan et al (Prospects for cationic polymers in gene and oligonucleotide therapy against cancer, Advanced Drug Delivery Reviews, 2002. 54:715-758) teaches gene therapy utilizing cationic polymers are viable ways with tremendous potential for treating cancer (see abstract). Merdan teaches that strategies for cancer gene therapy treatments include the "manipulation of gene expression either on the transcriptional or on the translation level" and "a deficient gene can either be replaced or the effect of an

unwanted gene can be blocked" (page 717, Column I, Introduction Section). Merdan teaches that polycations are able to complex with polynucleotides such as DNA plasmids, antisense oligonucleotides and RNA (see figures 1 and 4). Merdan teaches that the vector/nucleic acid complex is delivered to the target tissue, where it is taken into the cell for further processing (page 722, column I, section 3). Once inside the cell the DNA or RNA component of the polyplexes has to reach the site of action in the cell (page 735, section 3.2.5). Merdan teaches that the plasmid DNA "has to be transported into the nucleus, on order to exhibit the desired gene expression" but that ribozymes and RNA may function in the cytosol (page 735, section 3.2.5). Merdan further teaches that ribozymes are "RNA molecules endowed with catalytic cleaving mRNA molecules in a sequence specific, catalytic manner" (page 740, section 4.1.2).

26. A skilled artisan would have been motivated to combine the teaching of Meier on a composition comprising a polynucleotide and a polyvinylether with the teaching of Merdan on the benefits of using polycation/polynucleotide complexes for the treatment of cancer where the polynucleotide expresses a gene or an RNA because alteration of gene expression, either through up-regulation of a deficient gene by translation of the plasmid DNA into protein or down regulation of a gene through the expression of a ribozyme are both viable strategies for gene therapy. It would have been obvious to the skilled artisan to combine the teaching of Meier on a composition comprising a polynucleotide and a polyvinylether with the teaching of Merdan on the benefits of using polycation/polynucleotide complexes for the treatment of cancer where the polynucleotide expresses a protein or an RNA because the ultimate goal of gene

therapy is the alteration of endogenous protein levels- either through the addition of a deficient gene or protein, or the suppression of an overabundant gene or protein- thus by expressing the protein or the RNA are obvious limitations for the composition of the instant invention. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

Conclusion

27. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

kam/11/21/06

DAVID GUZO
PRIMARY EXAMINER